Solving drug related problems of older patients with polypharmacy discharged from the hospital

Ahmad, A.

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General discussion

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Deficiencies in the transfer of information of medication regimens and changes therein made during their stay in hospital are well known risk factors for the occurrence of drug-related problems (DRP) in older patients returning to home care after hospital discharge[1-4]. Of these patients many are specifically at risk as the result of multiple chronic morbidity and a reduced vitality[5;6]. The main focus of the present thesis is to study the effect of a clinical medication review (CMR) and patient counselling by community pharmacists, pharmacy technicians and general practitioners (GP) on the occurrence of DRP among older patients using multiple drugs for the treatment of a chronic disease discharged from hospital. Reducing existing and potentially avoidable medication errors resulting in DRP among these patients is essential to improve the effectiveness of their pharmacotherapy, ensure their safety and prevent rehospitalisation.

In the present thesis the effect of a CMR consisting of a medication analysis, a treatment analysis, a patient interview and counselling after hospital discharge, on the occurrence of DRP in older patients with polypharmacy after hospital discharge was studied. We developed a practicable, structured and comprehensive patient-centered tool for pharmacists to conduct a CMR including a checklist of commonly occurring (potential) DRP specific for this group of older patients. The perspective of the patient is introduced by means of a patient interview yielding essential information on patients' beliefs, satisfaction with information received about the medication and adherence to treatment. The effect of the CMR on health care utilization and associated costs, particularly those brought about by rehospitalisation was also studied. This final chapter contains a summary of the main findings of our studies, followed by a discussion of the methodological considerations of the various studies included in this thesis. Finally, the implementation of the CMR in clinical practice according to the RE-AIM model for implementation is discussed.

Main Findings

DRP are problems associated with drug treatment that may lead to rehospitalisation, increased morbidity and increased mortality[5;6]. Particularly in older patients with co-morbidities and polypharmacy discharged from hospital the risk on the occurrence of DRP is substantially increased[7-10]. Hospitalisation and hospital discharge, a rather frequent phenomenon among these patients, is often accompanied with (unintentional) changes in the medication regimen[1;2]. These changes substantially increase the likelihood of medication errors like the introduction of inappropriate drugs and drug-drug interactions[11-13]. Hospitalisation and discharge are also associated with discontinuity of care, inadequate patient information and deficits in communication[3;14;15]. Thus, at discharge the use of certain drugs may have been discontinued, doses of other changed and new medication may have been added. Moreover, first-line caregivers and patients may not exactly know which

medicines should be used while patients may not have been adequately informed about their medication and its use.

Chapter 2 of the thesis concerns a descriptive study on the prevalence of DRP in older patients with multiple chronic morbidity and polypharmacy discharged from hospital. It was the aim to distinguish different categories of DRP. This may help health care workers to target (potential) DRP. In order to identify and categorize DRP a specific review tool including a checklist of frequently occurring DRP and a script for a patient interview was developed. In this study nearly 95% of the patients was related to at least one DRP. The most common DRP identified were 'no drug but existence of a clear indication', 'unnecessarily long duration of treatment', 'too low dose of drug' and an 'incorrect drug choice'. DRP most often experienced by patients identified by means of the patient interview were ´side effects´ and ´lack of knowledge of the drugs prescribed´. The number of drugs used per patient was associated with the number of DRP occurring[16;17]. Patients with type 2 diabetes mellitus had significantly more DRP than patients without the disease. The most common DRP in these patients was 'no drug but clear indication', mainly due to the absence of a cholesterol lowering drug in their medication. Patients discharged from the pulmonary departments had on average more DRP as compared to patients discharged from other hospital units.

Chapter 3 describes the design of a randomized-controlled trial to study the effects of a CMR on the occurrence of DRP in older patients with multiple chronic comorbidity and polypharmacy after hospital discharge, adherence to post-discharge medication, re-hospitalisations and costs. The trial was conducted in 23 community pharmacies in Amsterdam, Amstelveen, Hoofddorp and Diemen. Participating pharmacies were randomized in an intervention and control group. The medication of patients in the intervention group was reviewed by their community pharmacist using the full record of prescription-only drugs and the patients' medication evaluation profile.
Assessment of these documents was supported data obtained by using a specifically developed tool consisting of a comprehensive checklist of 126 frequently occurring DRP and a semi-structured interview script for a patient interview (chapter 6). The prevalence of DRP of patients of control and intervention pharmacies was assessed at base-line and at 12 months by two experienced clinical pharmacologists. With use of the semi-structured patient interview specifically trained pharmacy technicians identified patient-experienced DRP at different times after discharge. Patients of control pharmacies received usual care according to the Dutch Pharmacy Standard. Secondary objectives of the study included: adherence with drug treatment as assessed by using the Medication Adherence Rating Scale (MARS), incidence of rehospitalisation, results of the beliefs about medication questionnaire (BMQ), outcome of the patients satisfaction with information about their medication questionnaire (SIMS) and the cost-effectiveness of the intervention.

The main objective of **chapter 4 and 5** was to examine whether the pharmacist-led CMR was effective in reducing the occurrence of DRP in older patients with polypharmacy after hospital discharge. Results from the randomised-controlled study show that the CMR is an effective method to reduce DRP. In the intervention group the proportion of patients with DRP was significantly reduced, especially the categories 'no drug but clear indication', and 'fear of side effects'. The intervention was particularly effective in patients with heart failure or hypertension.

Chapter 6 describes the development of a practicable, structured and comprehensive medication review tool for use by pharmacists and GP. The medication review tool consists of a comprehensive checklist of 126 DRP divided into 20 sections according to physiological system and disease, respectively, and includes a semi-structured interview script for a patient interview. The script enables pharmacists and GP to identify DRP and include the perspective of the patient in the checklist as required for a CMR.

Chapter 7 deals with patient-reported outcomes of the randomized controlled trial. The main research question was the possible existence of a relationship between beliefs about medication and the information received about medication and adherence. Older patients with polypharmacy discharged from hospital strongly believed in the necessity of using their medication. They were less concerned about the possible risk of using their drugs. They were also fairly indifferent to the idea that their medicines would be addictive had less negative beliefs about their medicines to be addictive, but had more negative views on the possibility that their doctors were using too many drug for their treatment. All patients were satisfied with the information received by their pharmacist about their drugs. Beliefs and information received indeed were associated with adherent behaviour among patients.

Chapter 8 investigates the effect of CMR on health care utilization and to investigate whether CMR is a cost effective method to reduce DRPs in older patients with polypharmacy discharged from hospital. CMR led to a non significant reduction in DRPs, higher costs and a significantly higher rate of hospital readmissions. Although we had limited power, we conclude that the intervention therefore proved not cost effective.

Methodological considerations

In order to interpret the findings of this study, the limitations and strengths of the study must be acknowledged. Adjustments made to the protocol and other methodological considerations of the different studies in this thesis will also be discussed in the following sections.

Adjustments' to the protocol

Three adjustments to the protocol were made (chapter 3). Initially, the impact of the intervention would be analyzed by means of multilevel linear regression analyses in order to allow clustering of observations of participants receiving care from the same pharmacy. However, due to various reasons some pharmacists of intervention pharmacies failed to conduct the CMR as intended and a substantial part was conducted by the same clinical pharmacist, who was a member of the research team. Although this showed that the intervention was not easily implemented in the participating intervention pharmacies, it was therefore not necessary to take account of this phenomenon (multilevel regression analysis) in our analysis. A second adjustment was that the effects of the CMR and patient counselling on adherence to drug treatment were not evaluated. The study protocol provided for an assessment of the effects of Motivational Interviewing and Problem Solving Treatment on adherence behaviour. Unfortunately, it was impossible to accurately establish the extent to what pharmacists and pharmacy technicians applied this tool in counselling their patients and to properly process the available results. However, at baseline, as measured by means of the MARS, all patients appeared highly adherent with the use of their medication. We therefore decided to cancel the evaluation of the effects of CMR and patient counselling on patients' adherence.

The final adjustment concerned the lack of complete and/or useful data obtained from the questionnaires as returned by the patients who participated in the study. Moreover, it also appeared that only a limited number of pharmacies had given these questionnaires to their patients. Regretfully, the absence of sufficient suitable data prevented a sound analysis of all secondary objectives described in the initial study design (i.e. functional status, adherence with drugs by rates of refilling prescriptions, patients' quality of life and the appropriateness of medication regimens of intervention and control patients and the acceptability of the pharmacists and GP with the method used during the research).

Methodological considerations of the studies, measurements

The intervention: clinical medication review

Studies aimed at improving medication safety by integrating a medication review component are usually difficult to design. The most preferred design, a controlled double-blind randomized study at patient level, is not suitable to study these interventions. This is mainly caused by the fact that the number of pharmacists and pharmacy technicians having the skills to readily conduct a medication review is limited. Pharmacy staff usually requires additional training in order to adequately conduct a CMR. Since we also aimed to minimize the possibility that randomisation at patient level would also lead to improved patient treatment by control pharmacists we choose to randomize

at pharmacy level. As a consequence only pharmacists and pharmacy technicians who were randomized into the intervention group were specifically trained to conduct a CMR. However, in spite of our efforts, in practice many pharmacies of the intervention group failed to review the medication records of all patients as intended, largely because pharmacists felt that there was a lack of time or there were insufficient trained pharmacy technicians available. Instead, the medication records of the majority of patients were reviewed by an experienced clinical pharmacist who was a member of the research team. As the result, a multilevel analysis was not necessary, and instead regression analysis was conducted.

After randomizing at pharmacy level, the pharmacies became aware whether they were randomized to the intervention or control pharmacy groups. Control pharmacists therefore might have been more aware of the possibility that their patients might experience DRP and become more observant and active in resolving DRP, this may have led to an underestimation of the effect of the CMR on the occurrence of DRP among patients in the intervention group. In order not to influence the data of our study, the clinical pharmacists who supported the intervention pharmacies and conducted medication reviews and other CMR activities at baseline and at follow up were blinded. They therefore did not know which patient belonged to which pharmacy. The patient information on drug use did not include a pharmacy number, since it would indicate that a certain patient belonged to an intervention or a control pharmacy. During the interview at baseline the researchers knew whether they interviewed a patient from the intervention or control pharmacy. However, after follow up, the researchers interviewed the patients again but they did not know whether they interviewed a patient from a control or an intervention pharmacy.

The intervention and control groups were similar with respect to demographic characteristics. Patients in both groups had an average of three chronic diseases. The intervention and control groups were not comparable with respect to the number of DRP. There was a significant difference in the number of DRP experienced by the patient at baseline between the intervention and control group. DRP experienced by patients of an intervention pharmacy might have been recorded more carefully. For this reason, we adjusted for the difference in DRP at baseline. Eventually 180 patients were enrolled in the intervention group and 160 patients in the control group. For about 75% of the patients in the intervention group a full CMR, including medication analysis, treatment analysis and patient interview at baseline and after one year of follow-up, was conducted. This percentage was similar in the intervention and the control group The trial was evaluated using an intention to treat methodology.

We expected no effects caused by differences in the treatment by GP and specialists, because the pharmacists in our study were randomized within the framework of a pharmacotherapeutic audit meeting (PTAM). At PTAM meetings agreements are made to improve the pharmaceutical care provided. A PTAM-group generally consists of two to six pharmacists from two to three pharmacies and six to ten GP with practices in the same area. Because we randomized within a PTAM

the distribution of patients in the control and intervention pharmacies, GP and specialist from one area were similar. In conclusion, in spite of several difficulties with respect to the feasibility of conducting CMR, we showed that the intervention resulted in a reduction of the number of DRP. We therefore claim that the use of the tool including a checklist with common DRP in combination with the semi-structured patient interview increased the effectiveness of a CMR.

Validity of our tool

The tool used to identify DRP

In order to facilitate and support community pharmacists and GP in efficiently conducting a (periodic) CMR of the medication of elderly outpatients with polypharmacy, a structured, comprehensive but practicable tool was developed.

Tools and their limitations

In the literature several screening tools are described that can be used by physicians and pharmacists to screen the medication of older patients with respect to inappropriate prescribing. Over the years, substantial effort has been made to prevent and detect DRP[18-20]. Several sets of explicit criteria of which the Beers´ criteria are the oldest and best known, have been developed to assist caregivers in making appropriate drug choices or assessing the quality of medication[18;20;21]. These explicit criteria, occasionally combined with other measures, are also used as tools to conduct medication reviews[22]. Since their introduction in 1991 the Beers´ criteria and subsequently adapted sets in various countries have been revised and refined with respect to structure and comprehensiveness[18;21;23]. Of these the STOPP/START criteria in which several shortcomings of the original Beers' criteria list have been addressed, are the best known. Shortcomings particularly concerned the detection of undertreatment, the inclusion of drugs exclusively registered in the US and a classification of drugs that is not based on physiological systems or disease states[18;21;24]. Although a review of medication records solely on the basis of explicit criteria lists may be useful, the result in terms of detected DRP will be of limited value since medical status and clinical parameters have not been considered. Moreover, these evaluations do not take account of the way patients experience their treatment[19;25;26]. Therefore, only a medication review with direct input from the patient, the so-called CMR, addressing beliefs on convenience and effectiveness of treatment, and eventual discomfort due to adverse events as determinants of adherence, allows to balance medical necessity with the expectations and the physical and mental abilities of the patient to continue treatment in an effective, satisfactory and safe manner[19;25-27].

Tool designed for this study

In this study we developed a tool consisting of a checklist of 126 commonly occurring DRP and a script of a semi-structured patient interview used for the identification of patient-related DRP. The tool is intended as a practicable aid in the systematic process of gathering and evaluating data on the actual use of medicines used by older patients for the treatment of chronic diseases as required to conduct a CMR. The tool should support both less and more experienced professionals in efficiently conducting CMR. The tool was developed on the basis of a literature search and a content validity procedure in which experts appraised its comprehensiveness, accuracy and practicality. The tool was validated by testing its use by means of a randomized trial[28]. As yet, the implementation of the tool in daily practice has not been investigated.

Questionnaires

In the study described in chapter 5 questionnaires were used to obtain self- reported data on patient characteristics such as age, gender, marital status, education level and origin. These questionnaires were also used to obtain data about attitudes and satisfaction with the Beliefs about Medication Questionnaire (BMQ)[29] and Satisfaction with Information about Medication (SIMS)[30]. Patient self reported adherence was also assessed by means of the Medication Adherence Rating Scale (MARS)[31]. All questionnaires used in his study were validated. However these questionnaires were not specifically developed for the patient group participating in the studies of the present thesis. Therefore several limitations with respect to the validity of the questionnaire data have to be addressed. Firstly, questionnaires were delivered to the patients at the start of the study and after one year. Not all older patients included in this study were physically or mentally able to fill out both questionnaires, which resulted in incomplete data. Secondly, it is possible that patients are likely to report favourable answers on self-reported measures[32]. In this chapter the main outcome measure was the self-reported adherence of patients discharged from hospital. The self reported adherence was assessed using the MARS. Assessment of the actual drug use by using more objective measures such as pill counts or pharmacy reports would probably have been more accurate. The use of self-reported data has been shown to overestimate compliance by 30%[31]. However, self-report methods are more efficient and cost effective to assess adherence and this method was considered more convenient for older patients recently discharged from hospital. In the present study results of the MARS showed a skewed data distribution. Other studies have also showed skewed data distribution of MARS results[31;33]. For the comparison of adherent with patients who are not adherent dichotomization was applied. The cut-off point of the MARS varied from 20 to 25, although a clear cut off point has not been defined for the MARS. In our study and other studies most patients reported a very high adherence score. Since the MARS is widely used, this indicates that more research is needed to identify an appropriate cut off point. However, other studies used the same cut off point as in our study[34].

Cost diaries

In order to investigate whether application of CMR results in a reduction of health care costs (chapter 8), patients were asked to fill out cost diaries during a period of one year. These cost diaries informed the researchers about how many times patients in the intervention and control groups visited their GP, a specialist, or a physiotherapist or were visited by their GP. The second part of the cost diary was also used to assess re-hospitalisations. Patients were also asked if they received care from other health care professionals except those mentioned in the cost diary. Although patients were motivated to participate and fill out these cost diaries each month, most of the data from the second part were missing. We suppose that filling out this part of the cost diary was too much work for the patients, because there were too many cost data entries. In addition, the diaries may not have been sufficiently legible (of understandable) for the patients. Furthermore, this study included elderly patients with chronic disorders, who already are more likely to forget to regularly fill out the cost diary. A more efficient method would have been to contact the hospitals and ask for information on rehospitalisation.

Feasibility

Complex Intervention according to the REAIM model

We included almost 70% of older patients with multiple chronic morbidity and polypharmacy discharged from hospital into the study. Patients who declined to participate generally felt too ill to participate. This may have led to an underestimation of the number of DRP identified. Although we intended to include patients from all origins, 97% of the patients in our study were of Dutch origin. According to the Dutch Central Statistics Office (CBS), about 40% of patients living in urban areas are not of Dutch origin[35]. Our results are therefore not representative for ethnic minorities/ groups living in the study area.

A CMR is a complex intervention, consisting of a medication analysis, a treatment analysis, a patient interview and counselling. In this trial we were dependent on the expertise, knowledge and skills of the participating pharmacists, pharmacy technicians and GP, as well on the checklist developed to identify commonly occurring DRP and its use by these caregivers. Conducting a CMR took substantial time from the pharmacists. Not only DRP had to be identified, but also GP should be contacted in the case that there was a need to discuss specific DRP or changes in the medication. Pharmacy technicians were trained in interviewing and counselling patients to identify DRP. Some pharmacy technicians may have the capacities to identify more DRP than others. To minimize these differences a structured interview script was used. In daily practice it appeared that there were not enough trained pharmacy technicians to interview patients. In addition, the intervention was implemented in the same time that pharmacies were subjected to serious budgetary restric-

tion measures. These measures caused major logistic changes of the working process in community pharmacies leaving them less time to conduct interventions aimed at improving patient safety. However, whatever twist or turn is taken, carefully conducting a CMR in a community pharmacy is a process that takes considerable time. It not only requires the full attention of the pharmacist, pharmacy technicians and each patient´s GP but also considerable organizational skills of the pharmacist in other to ensure a smooth collaboration between these health care workers. Maintaining the study design under these difficult conditions required a certain level of support for the pharmacists. Therefore, in our study a clinical pharmacologist, who was a member of the research team conducted several medication reviews while researchers of the project supported the pharmacies with various other intervention activities.

Future Implications

The study shows that a CMR reduces DRP in older patients with multiple morbidity and polypharmacy discharged from hospital. However, the implementation of a CMR by pharmacies and GP as a routine intervention in daily practice will be difficult and further measures facilitating this process should be devised and evaluated. Despite training in applied pharmacotherapy and communication skills community pharmacists often lack experience to efficiently conduct CMR. Patients whose medication most urgently requires regular CMR are elderly with multiple chronic disorders and polypharmacy[4]. In order to support pharmacies in conducting CMR, we developed a specific tool which comprises of a checklist of commonly occurring DRP and a script for a semi-structured patient interview allowing pharmacists to rapidly identify DRP. As such the tool proved easy to use and its application prevented omissions in the detection of DRP. However, for a more efficient and widespread use of the tool, in particular the registration of DRP and pharmacists' and GP' actions, the tool should be computerised and integrated in pharmacy information systems. Saving time in particular would facilitate the spread of the CMR process since, in addition to inadequate skills, in the study a lack of time proved another impediment of conducting the intervention leaving the patient interview and subsequent counselling the most time consuming elements.

Adequate pharmaceutical care for older patients also requires a good cooperation between pharmacist and GP. It is unclear whether the present level of collaboration between pharmacists and GP is sufficiently developed to adequately conduct CMR on a routine basis. As discussed elsewhere, the collaboration between pharmacist and GP is often less than optimal largely because of differences between their responsibilities, focus background, personalities facilities while both have a limited availability of time[36]. A CMR can only be successfully conducted when both pharmacists and GP are used to work closely together in a structured but informal manner.

In conclusion, a CMR consisting of medication analysis, treatment analysis and patient interview resulted in a reduction of DRP in older patients with multiple chronic morbidity and polypharmacy

discharged from hospital. It is important to identify and prevent DRP experienced by patients after discharge from hospital, because these problems may interfere with patient beliefs about medication use and therefore influence the adherence behaviour of older patients. Emphasizing the importance of using drugs for patients' health and reducing negative beliefs about drugs being overused by doctors can stimulate the adherence of older patients using several drugs for chronic use. Although the use of a tool which was specifically developed to support the conduct of a CMR may facilitate this complex element of pharmaceutical care, possible solutions to remove the various barriers that impede a full implementation of CMR as a routine intervention in daily practice should be found and evaluated. We found that a CMR was not cost effective in this vulnerable patient group. In order implement CMR different implementing strategies should be explored. In addition, specific interventions aimed at the reduction of hospitalisations should be developed.

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